**CASE STUDY**

**M. Kansasi** pulmonary disease in idiopathic CD4+ T-lymphocytopenia

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**ABSTRACT:** Cases of patients with markedly depressed CD4+ T-lymphocyte counts, with or without opportunistic infections, in the absence of any evidence of human immunodeficiency virus (HIV) have been described in recent years. In 1992, the definition of "idiopathic CD4+ T-lymphocytopenia" was formulated by the Centers for Disease Control and Prevention (CDC) of Atlanta (USA).

The present case illustrates the occurrence of an unexplained Mycobacterium kansasii pneumonia in a white HIV-negative subject with a persistent depletion of CD4+ T-lymphocytes and suppression of cell-mediated immunity.

To our knowledge, this is the first observation of idiopathic CD4+ T-lymphocytopenia with pulmonary mycobacteriosis due to Mycobacterium kansasii, and the sixth case of this kind of immunodeficiency described in Italy.


Since 1989, unusual cases of opportunistic infections and CD4+ T-lymphocytopenia in the absence of human immunodeficiency virus (HIV) infection have been reported. In 1992, the Centers for Disease Control and Prevention (CDC) of Atlanta (USA) published a provisional case definition based on the documented depletion of CD4+ T-lymphocytes, and the absence of HIV infection and other types of defined immunodeficiency. A further epidemiological investigation carried out by the CDC led to an improved definition of the syndrome and stressed its extreme rarity: only 2 out of 230,179 patients entered in the CDC Acquired Immune Deficiency Syndrome (AIDS) Reporting System fitted the case definition. Until the end of 1992, only 49 cases had been classified as idiopathic CD4+ T-lymphocytopenia (ITL) in the United States. According to recently acquired knowledge: this syndrome is not new (cases have been identified as far back as 1983); it is not caused by HIV-1, HIV-2, human T-lymphocyte virus (HTLV) I, or HTLV II; it is heterogeneous; it is epidemiologically, clinically and immunologically somewhat different from HIV infection; and it does not appear to be caused by a transmissible agent [1, 2].

**Case report**

In April 1989 we first observed a 29 year old Caucasian male with radiological features suggesting pulmonary tuberculosis (TB). He was an officer of the Italian Navy Diving Corps submitted to a routine annual chest roentgenogram. The patient was, to all appearances, well and completely symptom-free. He had no risk factors for HIV infection and had not received immunosuppressive therapy or blood transfusions in the past. Chest radiography and tomography showed a wide micronodular infiltrate in the upper lobe of his right lung, where a 2.5 cm large parahilar infiltrate was also present, and a smaller contralateral infiltrate. Intradermal reactions with purified protein derivative (PPD) 5, 10 and 100 international units (IU) (Sclavo test PPD; Sclavo Laboratories, Siena, Italy), and the multitest for cell-mediated immunity (Multitest IMC Merieux) were completely negative, whilst the serological assay of antibodies to the mycobacterial antigen-60 (A60) (TB-test; Eurospital S.p.a., Trieste, Italy) revealed the presence of specific immunoglobulin M (IgM) but not immunoglobulin G (IgG), so that a provisional diagnosis of tuberculosis was made in accordance with the guidelines for the interpretation of serology with A60 [3, 4].

Fibrebronchoscopy with bronchial lavage (BAL) was performed. The BAL fluid was cultured on Stonebrink, Lowenstein-Jensen and Gottskasser mediums, and a Mycobacterium kansasii strain was isolated. In vitro sensitivity testing for antimycobacterial drugs was not performed. Identification of M. kansasii was further confirmed on a specimen from a bronchial biopsy, both by Ziehl-Neelsen staining and a positive culture. A protocol of antimycobacterial therapy with four drugs (rifampicin (RMP) + isoniazid (INH) + ethambutol (ETB) + streptomycin (SM)) was initiated.

During the first 10 months, some improvement was observed in the radiological lesions, with a partial collapse of the pulmonary cavity and an initial evolution of the micronodular infiltrates toward fibrosis. In April 1991, a relapse occurred, with reactivation of all the previously seen infiltrates. Since October 1991, the radiological features have stabilized, suggesting a definitive evolution to pulmonary fibrosis.

The immune profile was monitored from May 1989 to December 1993. The search for antibodies to HIV-1...
and HIV-2 (Abbott-Elisa) was always negative and a Western Blot (Pasteur Institute, Paris, France) was also negative. The patient’s wife was tested twice, at the beginning and 6 months later, with negative results. A recently performed polymerase chain reaction (PCR) (Amplicor HIV; Roche, Basel, Switzerland) confirmed the absence of HIV infection in the patient. The serological assays for Cytomegalovirus, Epstein-Barr virus, HTLV-I and HTLV-II-infections were also negative.

The CD4+ cell counts were persistently low, ranging 246–385 cells·mm-3; on the first two observations, the count was below 300 cells·mm-3 (fig. 1). Moreover, on only one occasion did the CD4+ cells represent more than 20% of total lymphocytes. The proliferative responses of T-cells in vitro to mitogens (phytohaemagglutinin) were tested in October 1989 and in February and June 1990, and were depressed (20,000, 35,000 and 22,650 cells·mm-3, normal value 86,200±29,412 cells·mm-3). The cell-mediated immunity (CMI) multitest showed a complete absence of response to all seven antigens throughout the entire follow-up. Serum immunoglobulin levels always remained within the normal range.

Discussion

HIV-seronegative patients with some clinical evidence of AIDS have been observed in the past. A survey of 230,179 cases of AIDS reported to the AIDS Reporting System of the CDC [1] initially revealed 299 HIV-seronegative patients, but a further evaluation of these cases led to most of them being reclassified as HIV-positive or afflicted by some other type of defined immunodeficiency. As mentioned in the introduction, only two patients fitted the provisional case definition of idiopathic CD4+ T-lymphocytopenia (ITL), which included the following: a documented absolute CD4+ T-lymphocyte count of less than 300 cells·mm-3 or less than 20% of total T-cells on more than one occasion; no evidence of infection on HIV testing; and the absence of any defined immunodeficiency or therapy associated with depressed levels of CD4+ T-cells. Another 47 patients with ITL have been described in the USA. All of them presented clinical conditions which remained stable over time, less than 50% had risk factors for HIV infection, and they did not have hypergammaglobulinaemia, which is so common in HIV-infected patients. In the majority, the CD4+ T-cell counts remained stable over time, and in several patients there was a spontaneous reversal toward normal. Some also showed decreased numbers of CD8+ T-cells and B-cells. None of them revealed any evidence of HIV-1, HIV-2, HTLV-I, HTLV-II or other mononuclear-cell-tropic virus [1, 5]. All close contacts and sexual partners who have been studied were clinically well, and showed no sign of immunological abnormality or evidence of HIV infection. Five patients had pulmonary mycobacteriosis; three caused by Mycobacterium tuberculosis, two by Mycobacterium avium complex, and one of the latter two also had a Mycobacterium chelonii pneumonia. Three patients had extrapulmonary Mycobacterium avium complex disease.

We initially classified our patient as having a form of anergic tuberculosis. However, after the isolation of Mycobacterium kansasi from his lungs and observation of his immune profile, we considered the possibility that this was a case of so-called "HIV-seronegative AIDS". Reconsidering his entire history in the light of recent information about ITL, it was observed that he corresponded perfectly to the CDC definition: he presented with pulmonary mycobacteriosis; he had CD4+ T-cell counts of less than 300 cells·mm-3 on more than one occasion; there was no evidence of HIV or other viral infection causing immunosuppression; he presented no other type of defined immunodeficiency; he had never taken immunosuppressor drugs, or received blood transfusions. Furthermore: he had no risk factors for AIDS; his sexual partner had never shown evidence of HIV infection; his clinical condition never deteriorated, although his response to antimycobacterial therapy was not completely satisfactory; his CD4+ T-cell counts remained stable over time, and at the end of monitoring showed a tendency toward recovery, without however reaching the threshold of 400 cells·mm-3; his CMI remained depressed; and immunoglobulin levels remained within the normal range. All of these characteristics led us to differentiate his condition from AIDS, common variable immunodeficiency [6–10], and mycobacteria-induced specific immunosuppression [11, 12].
As far as we are aware, this is the first observation of idiopathic CD4+ T-lymphocytopenia with pulmonary mycobacteriosis due to *M. kansasii*, and the sixth case of this syndrome described in Italy [13, 14].

We conclude that idiopathic CD4+ T-lymphocytopenia must be considered in all human immunodeficiency virus seronegative anergic patients with pulmonary or extrapulmonary tuberculosis or mycobacteriosis, and an accurate study of their immune profiles is therefore mandatory.

References


